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The Physiological Action of Chrysotoxin.

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(*Preliminary communication.*)

Chrysotoxin is the active substance obtained from ergot by Jacobi[1]. The specimens used have been prepared for me by Dr G. Barger, in conjunction with whom experiments are in progress on the nature and state of combination of the active constituents of this and other preparations from ergot. The substance was administered intravenously, as the sodium compound, in alkaline saline solution, the proportion of chrysotoxin being usually 1 %. The animals used were chiefly cats, which were anæsthetised with ether or pithed. The phenomena here to be described were observed in the cat, details of the reaction of other species being left for fuller publication.

The effects may be divided into

1. *Stimulation effects.* The work on these is as yet incomplete, but in all cases in which the phenomena have been investigated the effects correspond to stimulation of the cranial and sacral autonomic, and also of the true sympathetic nerve supply, to all organs containing plain muscle. The rise of blood-pressure is marked and prolonged. In a pithed cat a rise from a pressure of 50 mm. to one of 180 mm. of mercury was obtained by injecting 50 mgs. of chrysotoxin. With a smaller dose—10 mgs.—the rise though not so high (40 mm. to 130 mm.) is very prolonged, lasting upwards of 30 minutes. With larger doses the effect passes off more rapidly for reasons made obvious by the next section. The heart-beat is increased in force and slowed in rhythm. The pupil shows a passing dilatation, and then slowly and steadily constricts to a slit, the nictitating membrane being meanwhile retracted and the eyeball bulged forward. The movements of the small intestine exhibit a fleeting inhibition, succeeded by a prolonged augmentation of tone and rhythm. The same is true of the urinary bladder and gall-bladder. Powerful contractions of the uterus are set up.

As to the point of application of these stimulant effects, it may be stated that the blood-pressure effect is unaffected by complete pithing of the spinal cord, but is entirely abolished by a dose of nicotine, which leaves the response to adrenalin unaltered, and by apocodeine in such

[1] *Arch. f. exp. Path. u. Pharmakol.* xxxix, p. 85, 1897.

quantity as reduces, but does not abolish, the effect of adrenalin. Removal of the superior cervical ganglion abolishes the preliminary dilatation of the pupil; and the subsequent constriction, while quite unaffected by pithing the brain completely, is immediately abolished by section of the ciliary nerves. All the evidence at present available points, therefore, to the ganglion cells—or the endings on them of the preganglionic fibres—as the site of the stimulus.

2. *Paralytic effects.* If a large dose of chrysotoxin be given to a cat (100 mgs. to a cat of 2 to 3 kilograms), it will be found that a further dose produces either no effect on the blood-pressure, or a fall. If, while the rise of blood-pressure produced by such a large injection still persists, adrenalin be given intravenously, a marked fall of blood-pressure occurs. With an ordinary dose (0·05 – 0·1 mg.) the fall lasts for two minutes or more; with a larger quantity it lasts longer. An exactly analogous effect is produced by injection of a small dose (0·5 – 1 mg.) of nicotine or by stimulation of the splanchnic nerves. The fall is accompanied by a simultaneous increase in the volume of a loop of intestine observed by a plethysmograph. When the blood-pressure has sunk again to the minimum, sympathetic stimulation by any method causes a small fall of pressure, which may be succeeded by a prolonged slight rise. Barium chloride produces a rise of blood-pressure as usual. It is clear, therefore, that the sympathetic vaso-constrictor nerve-endings have been paralysed. An examination of the sympathetic endings in other organs of the body has shown that the cardio-accelerator endings and those in the dilatator of the pupil are affected to a comparatively small extent, while no paralytic effect on the pilo-motor nerve-endings is apparent. Of the others examined, the motor sympathetic nerve-endings were all paralysed, while the inhibitory endings responded as usual to artificial excitation. The following have been examined.

Paralysed.	*Unparalysed.*
Motor endings in :—Spleen	Inhibitory endings in :—Small intestine
*Ileo-colic sphincter	Gall-bladder
Internal anal sphincter	Fundus of urinary bladder.
*Urethra and trigone of bladder	
Uterus	
*Retractor penis (dog).	

* These experiments were made in conjunction with Mr T. R. Elliott.

The cranial and sacral autonomic nerve-endings, whether motor or inhibitory, show no trace of paralysis. On the contrary, the weakening of tonic impulses which reach an organ through an antagonistic sympathetic supply, even when this latter still responds to artificial stimulation, enables the unmixed effect of stimulation of a cranial or sacral autonomic supply to be observed with unusual clearness. Stimulation of the vagus, for example, causes more perfect cardiac inhibition and much more marked intestinal augmentation than under ordinary conditions.

No evidence is at present available to indicate whether or no the same active principle is responsible for both stimulant and paralytic effects. The stimulant effects are evidently those ordinarily associated with the action of ergot. The paralytic effects furnish a new method of discrimination in cases where an organ receives both motor and inhibitory impulses from the sympathetic. The fall of blood-pressure with adrenalin, etc. may be due to vaso-dilatator fibres in the sympathetic system, ordinarily masked by predominant vaso-constrictors: but the possibility is not yet excluded of the effect being due to the relaxation of the muscular wall of the intestine, causing a passive dilatation of the intestinal vessels.